IN THE SPECIFICATION:

Please delete the subheading on page 1, and replace with the following:

~~DESCRIPTION OF THE STATE OF THE ART~~

--FIELD OF INVENTION--

Page 1, after subheading, please insert the following:

This application pertains to peptides that have antagonistic activity in preventing TGFβ1 from interacting with TGFβ1 receptors.

Page 6, after the last paragraph, please insert the following:

SUMMARY OF INVENTION

Peptides that are antagonists of the binding of TGFβ1 to its receptors in the body. The peptides are characterized in that they have partial amino acid sequences that are identical or similar to those of TGFβ1 itself and/or its receptors.

BRIEF DESCRIPTION OF THE DRAWINGS

Fig. 1. Inhibition of binding of TGFβ1 to the MV-1-Lu cells by peptide P144, measured by flow cytometry. A, image obtained on examining the cells incubated with biotinylated TGFβ1 and developed with avidin-FITC. B, image obtained on examining the cells incubated with avidin-FITC without prior addition of TGFβ1. C, image obtained on examining the cells incubated with TGFβ1 previously incubated with peptide P144 at a concentration of 0.42 μg/μl, and developed with avidin-FITC. The fluorescence emitted is shown on the abscissa, while the ordinate shows the number of cells for each value of fluorescence. The fields corresponding to the cells labelled with TGFβ1-biotin and avidin-FITC (M2) and to the unlabelled cells (M1) are also shown.

Fig. 2. Schematic representation of the process of cirrhosis by CCl_4. Black arrows indicate when two weekly doses of CCl_4 were administered to the rats, and black dashed arrows show when there was one weekly dose. The grey arrows indicate administration of peptide P144. A: Healthy controls; B: Healthy controls + P144, B_1: with peptide 70 μg/day; C: Cirrhotic; C_1 with saline; C_2 with peptide 70 μg/day; D: Cirrhotic with CCl_4 + phenobarbital; D_1 plus saline; D_2 plus peptide 70 μg/day.

Fig. 3. Effect of TGFβ1 on growth of MV-1-Lu cells. The cells are cultivated at a density of 5000 cells/well at

the concentrat ıs of TGFβ1 indicated, pg/ı Abscissa: TGFβ1 concentration (pg/ml); Ordinate: c.p.m.

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Fig. 5. Percentage inhibition of the activity of TGFβ1 (200 pg/ml) in the presence of various nominal concentrations of peptide P12, filtered (◆) and unfiltered (•).

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Fig. 8. Autoradiograph of an affinity labelling test of the receptors of TGFβ1. Lanes C1 to C6: effect of preincubation of the MV-1-Lu cells, with different concentrations of peptide P29 (10^6, $8x10^5$, $6x10^5$, $4x10^5$, $2x10^5$ and 10^5 times the molar concentration of ^{125}I-TGFβ1 respectively), prior to addition of ^{125}I-TGFβ1. Lane C7: effect of preincubation of the MV-1-Lu cells with unlabelled TGFβ1 (10^2 times the molar concentration of ^{125}I-TGFβ1) prior to addition of ^{125}I-TGFβ1 (negative control). Lane C8: effect of incubation of the MV-1-Lu cells with a concentration of 0.42 µM of ^{125}I-TGFβ1, corresponding to an activity of 0.4 µCi, without prior preincubation (positive control).

Fig. 9. Percentage inhibition of TGFβ1 (200 pg/ml) by receptor peptides predicted as complementary to regions of TGFβ1. All the peptides were tested at a concentration of 200 µg/ml. Inhibition of TGFβ1 of 100% corresponds to the growth of MV-1-Lu cells that is obtained in the absence of TGFβ1.

Fig. 10. Percentage inhibition of TGFβ1 (200 pg/ml) by overlapping peptides derived from the extracellular region of the type III receptor. All the peptides were tested at a concentration of 200 µg/ml. Inhibition of TGFβ1 of 100% corresponds to the growth of MV-1-Lu cells that is obtained in the absence of TGFβ1.

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Fig. 14. Percentage inhibition of TGFβ1 (200 pg/ml) by receptor peptides derived from modification of peptide P54 (P139 to P143) and of the peptides derived from the human type III receptor (P144 and P145). All the peptides were tested at a concentration of 200 µg/ml. Inhibition of TGFβ1 of 100% corresponds to the growth of MV-1-Lu cells that is obtained in the absence of TGFβ1.

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to the cell receptors both by peptide P147 and by the non-radioactive TGFβ1.

Fig. 17. Percentage inhibition of TGFβ1 (200 pg/ml) by peptides derived from human type II receptor (P146), from fetuin (P147 to P149) and from endoglin (P150 to P154). All the peptides were tested at a concentration of 200 μg/ml. Inhibition of TGFβ1 of 100% corresponds to the growth of MV-1-Lu cells that is obtained in the absence of TGFβ1.

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Fig. 20. Effect of administration of peptide P144 on collagen synthesis during experimental cirrhosis induction with CCl_4. The ratio of collagen to total protein is shown on the ordinate. The abscissa shows the various groups of rats: Co= healthy rats; Co+P144= healthy rats treated with peptide P144; Tto_1= rats subjected to induction of cirrhosis with CCl_4 and administered peptide P144 on alternate days during this period and Ci_1= rats subjected to induction of cirrhosis with CCl_4 for 11 weeks and not treated with peptide P144.

Fig. 21. Effect of administration of peptide P144 on collagen synthesis during experimental cirrhosis induction with CCl_4. The ordinate shows the ratio of the area of fibrosis to the total area in tissue preparations stained with Sirius Red. The abscissa shows the various groups of rats: Co= healthy rats; Co+P144= healthy rats treated with the peptide; Tto_1= rats subjected to induction of cirrhosis with CCl_4 and administered peptide P144 on alternate days during this period and Ci_1= rats subjected to induction of cirrhosis with CCl_4 for 11 weeks and not treated with peptide P144.

Fig. 22. Effect of administration of peptide P144 on collagen synthesis once cirrhosis has been induced with CCl_4. The ordinate shows the ratio of collagen to total protein. The abscissa shows the various groups of rats: Co= healthy rats; Co+P144= healthy rats treated with the peptide; Tto_2= rats subjected to induction of cirrhosis with CCl_4 and administered peptide P144 on alternate days at the end of this period and Ci_2= rats subjected to induction of cirrhosis with CCl_4 for 11 weeks and not treated with peptide P144.

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Page 7, please delete the subheading and replace with the following:

~~DETAILED DESCRIPTION OF THE INVENTION~~

--DETAILED DESCRIPTION--

Please delete pages 40 - 47 starting with the subheading "DESCRIPTION OF THE FIGURES".

DESCRIPTION OF THE FIGURES

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